

45. The method of claim 16, wherein the physiologically acceptable gas is  $C_2F_6$ .
46. The method of claim 16, wherein the physiologically acceptable gas is  $C_4F_8$ .
47. The method of claim 16, wherein the physiologically acceptable gas is  $C_4F_{10}$ .
48. The method of claim 16, wherein the physiologically acceptable gas is  $SF_6$ .

### REMARKS

Applicants have amended the original claims to divide them into separately patentable subject matter. The broad classes of this separately patentable subject matter include claims directed to making a contrast agent that has "stabilized microbubbles" (i.e., claims 1-7, 13-15, 18, 21, 23-26, 32, 35 and 37-42), making a contrast agent that has "microballoons" (e.g., claims 16, 17, 19, 20, 22, 27-31, 33, 34, 36, and 43-48), making a contrast agent via a "gas substitution method" (e.g., claims 2, 3, 18 and 21 to stabilized microbubbles and claims 19, 20 and 22 to microballoons), and making a contrast agent that has a gas mixture (e.g., claims 15, 18, 21, 23-26, 32, 35 and 37 to stabilized microbubbles and 17, 20, 22, 28, 29, 30, 31, 34, 36 and 43 to microballoons).

In making these amendments, no new matter was added to the claims and the claims were not broadened. Claim 1 was amended by deleting several separately patentable inventions, which were submitted in new claims 15-17. Two gases (i.e.,  $CCl_2F_2$  and  $CBr_2F_2$ ) were also deleted from the claims, further narrowing them. A typographical error was also corrected by removing "in" from claim 1. In new claim 29, which is based on original claim 9, the polymer choice "polystyrene" was deleted, thus narrowing the claim.

The only "addition" to claims was to original claim 13 and new claim 32, which is based on original claim 13, wherein "microbubbles" was substituted for "microvesicles", and new claims 33 and 34, also based on original claim 13, wherein "microballoon" was substituted for "microvesicle." However, this is a per se narrowing of the claims because the term "microbubbles" is defined as a narrower subset of "microvesicles" in the '774 specification, at, for example, column 1, lines 23-27, and the term "microballoon" is also defined as a narrower subject of "microvesicles" in the '774 specification at, for example, column 1, lines 23-27.

The claims are supported in the specification as follows:

Claims 1-7, 13-15, 18, 21, 23-26, 32, 35 and 37-42 are all directed to methods of making contrast agents that have "stabilized microbubbles." The '774 patent first defines these "stabilized microbubbles" (col. 1, lines 27-45 and col. 4, lines 35-43), then discloses the claimed methods of making them, both generally (e.g., col. 1, lines 47-53; col. 3, line 63 to col. 4, line 3), and specifically (e.g., col. 4, line 53 to col. 6, line 46; examples 4-6). Certain of the "stabilized microbubble" claims (i.e., claims 1, 4-7, 13-15, 23-26, 32, 35 and 37-42) are directed to making the contrast agents "in the presence of " the gas, which is disclosed at, e.g., column 4, lines 65-68 and column 5, lines 48-56. The methods of the "stabilized microbubble" claims directed to the use of surfactants (i.e., claims 4-7 and 23-26) are disclosed at, e.g., column 4, lines 35-41; column 5, lines 22-33; and examples 4-6 and 8. The subject matter of the "stabilized microbubble" claims directed to the contrast agents with a favorable  $\Delta P$  or a prolonged life (i.e., claims 3, 13, 14, 21, 32 and 35) is disclosed in the specification at, e.g., column 6, lines 14-46; column 6, line 56 to column 7, line 54; column 8, lines 1-27; and in examples 4-6 and 8. Finally, the claimed gases and mixtures of

gases are disclosed both generally (e.g., col. 7, lines 65-68), and specifically (e.g., examples 4-6 and 8; the claim 3 that was filed with the specification).

Certain of the claims relating to stabilized microbubbles are directed to a method of making with a "gas substitution method" (i.e., claims 2, 3, 18 and 21). This method is disclosed in the specification both generally (e.g., col. 4, lines 53-64), and specifically (e.g., col. 5, lines 1-47; col. 5, line 57 to col. 6, line 13).

Claims 16, 17, 19, 20, 22, 27-31, 33, 34, 36, and 43-48, are all directed to methods of making contrast agents that have "microballoons." The '774 patent first defines these "microballoons" (col. 1, lines 33-45), and then discloses the claimed method of making them, both generally (e.g., col. 1, lines 47-53; col. 3, line 63 to col. 4, line 3), and specifically (e.g., col. 4, line 53 to col. 6, line 46; examples 1-3 and 7). Certain of the "microballoon" claims (i.e., 16, 17, 27-31, 33, 34, 36 and 43-48) are directed to making the contrast agents "in the presence of" the gas, which is disclosed at, e.g., column 4, lines 65-68 and column 5, lines 48-56. The "microballoon" claims directed to the use of polymers (i.e., claims 27-29) are disclosed at, e.g., column 4, lines 32-35 and 42-51; and examples 1-3 and 7. The "microballoon" claims directed to the contrast agents with a favorable  $\Delta P$  and a prolonged life (i.e., claims 22, 33, 34 and 36) are supported in the specification at, e.g., column 6, lines 14-46; column 6, line 56 to column 7, line 54; column 8, lines 1-27; and in examples 1-3 and 7. The claimed gases and mixtures of gases are disclosed both generally (e.g., col. 7, lines 65-68), and specifically (e.g., examples 1-3 and 7; the claim 3 that was filed with the specification). Finally, the use of "dry precursors" in claim 30 is disclosed at, e.g., column 5, lines 1-22.

Certain of the claims relating to microballoons are directed to a "gas substitution method" (i.e., claims 19, 20 and 22). This method is disclosed in the specification both generally (e.g., col. 4, lines 53-64) and specifically (e.g., col. 5, lines 1-47; col. 5, line 57 to col. 6, line 13).

For ease of analysis, the new claims (i.e., claims 15-48) are introduced by a reference to the original claim from which they are based. The new claims that were added are all based on the original claims and simply reflect the dividing out of the different subject matter of the original claims into separate claims. No new matter was added and no broadening of the original claims was done.

Applicants believe that these claims are patentable for the same reasons that the original claims were patentable. They are supported in the specification as shown supra, and Applicants are not aware of any prior art that has all of the elements of the claims or which

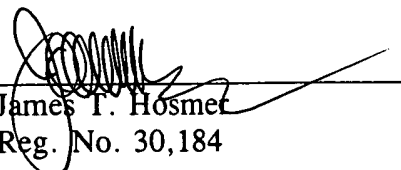
in proper combination with other prior art would provide all of the elements of the claims.

Thus, favorable action on these claims is requested.

Respectfully submitted,

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